made at that point. When the cecum cannot be mapped out by percussion or the subject is well developed, and even in all, the second plan is to note the position of the right edge of the rectus muscle on the umbilical-spine line maintaining the site with a finger. Having the patient rise to a sitting position helps in palpating for the rectus edge. Standing at the right and facing the patient (for right-handed individuals) the thumb is placed vertical on the abdomen, the tip of the thumb pointing to the ensiform, when it is slowly pressed backward into the abdomen, not inward, outward, up or down. When the thumb has been sunk about half-way down to the back of the abdominal cavity, it is swung to the right of the patient at a right angle to the downward pressure line. This pinches the appendix against the iliacus muscle and unyielding structures under and at the side of it, and usually elicits pain or tenderness. It is well, having done this in the mid-distance between the anterior superior spine and the umbilicus and not having obtained tenderness, to move the thumb down about one-half inch, performing it again, and so on downward until one has reached almost to the brim of the pelvis. The same procedure on the left side serves as a control. By means of this method of downward and then right lateral pressure it is possible to elicit tenderness in the average case of chronic appendicitis. When tenderness is obtained on transverse pressure to the left it may be a Lane's kink, and when below it may be a tender ovary instead of an appendix.

THE EFFECTS OF CONTINUOUS ADMINISTRATION OF EXTRACT OF THE PITUITARY GLAND.

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The present investigation was undertaken in order to study more particularly the effect of pituitary extract upon the blood pressure when administered by the mouth over a more or less prolonged period, but also, at the same time, to observe other phenomena which might be attributed to the employment of the drug.

The effect of intravenous or hypodermic injections of preparations of the pituitary gland upon the blood pressure has been studied by numerous observers, and the gland has been given by mouth for long periods in the treatment of infantilism; but in the first case the observations were only taken for a comparatively short time, and usually after one large or several frequently repeated doses, and in the latter case no systematic studies have been made of the effect of the prolonged use of the gland upon the blood pressure.

Various observers have shown that injections of extract of the infundibular portion of the pituitary gland cause a rapid and pronounced rise in blood pressure, which persists for a variable time, usually much longer than that produced by adrenalin, and which is due to the constriction of the peripheral arteries. Repeated injections, however, result in a less marked rise in the blood pressure after each injection until finally a fall in pressure occurs. Various theories might be employed to explain this fall:

1. That it is due to a saturation of the blood, with pituitary extract, "so that an interaction takes place which converts its constricting action on the peripheral vessels into a dilating one."[1]
2. That it is due to a late depressing action influencing the strength of the cardiac beat.[2]
3. That it is due to the action of the depressor substance which the gland contains overpowering the pressor substance, causing a dilatation of the peripheral bloodvessels.[3]
4. That it is due to the central dilator effect of the drug.[4]
5. That there is an inhibitory substance present, preventing a secondary action of the drug.[5]

Of these theories the first and second seem most tenable. It is therefore plausible to attribute the secondary depressor effect of the drug to the larger quantity that is necessary to produce this result. Similar effects are noted with some other drugs which in average dose will produce certain result, while larger, not necessarily lethal doses, will cause a result contrary to the initial finding. In giving fair-sized doses of the glandular extracts by the mouth the overwhelming action of the larger doses is thus obviated and the effects are largely those that result from its primary action. Aside from the action of the infundibular portion of the gland upon the vascular system, several other effects may be observed; thus it has been noted that persistent use of lager doses may cause glycosuria; after single and repeated intravenous injections diuresis occurs; frequently there is a slowing of the pulse rate, perhaps associated with a decrease in the amplitude of cardiac contractions; possibly an inhibition of the flow of pancreatic juice; and usually stimulation of the uterine and intestinal musculature. Clinically, the infundibular portion of the pituitary gland has been extensively employed as an oxytoxic, occasionally as a diuretic. It has given good results as a vasoconstrictor when employed in the treatment of shock and other conditions associated with transient low blood pressure. It has also been used in many other less relevant conditions. Extracts of the whole gland have been used in the treatment of both acromegaly and infantilism.

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[1] C. P. McCord, An Investigation of the Depressor Action of Pituitary Extracts, Arch. Int. Med., 1911, viii, 609.

[2] C. J. Wiggers, The Physiology of the Pituitary Gland and the Actions of its Extracts, AMER. JOUR. MED. SCI., 1911, cxli, 502.

[3] Schafer and Vincent, The Physiological Effects of the Pituitary Body, Jour. Phys., 1899–1900, xxv, 87.

[4] T. Sollman, and J. I. Pilcher, Central Vasomotor Effects, Jour. Pharm. Exp. Therap., 1910, i, 571.

[5] W. W. Hamburger, The Action of Intravenous Injections of Glandular Extracts and other Substances upon the Blood Pressure, Amer. Jour. Phys., 1904, xi, 282.

In the following series of patients the first few were selected for observation because they had showed persistent low blood pressure upon repeated examination; later, patients showing higher pressures were also given the glandular extract. In all, observations were made upon 18 people, 13 of whom were patients in the dispensary of the Hospital of the University of Pennsylvania, and 5 of whom were medical students who volunteered to assist in the investigation. The extract was given over a period of from one week to ten months without other medication. The 5 students took the extract for only a week, but it was administered to all the patients for at least a month unless stopped on account of some untoward effect. The preparation employed was the extract of the whole gland made up in 0.2 gram tablets containing 0.065 gram of the dried gland, equivalent to 0.26 gram of the fresh gland. The dosage at first was two of these tablets twice a day, but no effect was noted until the dose was increased to one tablet four times a day. Larger doses were given to several individuals, but soon discontined.

Although most observers have agreed that the posterior lobe or infundibular portion of the gland elaborates the secretion that acts upon the bloodvessels, nevertheless in a recent work, D. Lewis, J. L. Miller, and S. A. Matthews[6] found that extracts of the pars intermedia caused a decided rise in blood pressure, the extracts of the pars nervosa also caused an eventual rise in the pressure, as did likewise in the majority of instances, extracts of the anterior lobe. They believe that the pressor substance is secreted by the pars intermedia and those cells of the anterior lobe which bound the cleft. It therefore seemed feasible to employ the whole gland not only because of the impossibility of securing preparations containing only the pars intermedia, but also because the dried extract is more suitable to prescribe to dispensary patients.

The blood pressure was taken one or more times before giving the pituitary tablets, and then later at each subsequent visit to the dispensary until the observations were discontinued. The blood-pressure readings were all taken two or more hours after ingestion of the glandular extract and after half-hour or more rest in the dispensary. The readings were made by the auscultatory method, systolic and diastolic pressure being recorded while using a Stanton sphygmomanometer.

Patient 1.—The glandular extract caused a rise in pressure from 12 to 20 mm. of mercury in all the many observations. The pulse pressure showed but little variation. The pulse rate averaged consistently about 80 beats per minute, except at one time when it fell to 60, after taking larger doses, six tablets a day, for several days. This larger amount also caused diarrhea. Twelve days after cessation of treatment, pressure showed but slight change, in nineteen days it had returned to its former level.

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[6] The Effects on Blood Pressure of Intravenous Injections of Extracts of the Various Anatomic Components of the Hypophysis, Arch. Int. Med., 1911, vii, 785.

Patient 2.—The systolic pressure increased 18 mm. of mercury. The diastolic pressure was unchanged. Diuresis was observed.

Patient 3.—The systolic pressure was increased from 9 to 20 mm. at different observations. The pulse pressure was unchanged. A slowing of the pulse rate—60 per minute—was also noted for a short time. At one time during the experiment the patient stopped the drug for six days without any effect on the blood pressure. Eight days after the complete cessation of ingestion of the glandular extract the systolic pressure had returned to within 8 mm. of mercury of the average pressure before the experiment, and in thirteen days had fallen back to the previous average pressure.

Patient 4.—The systolic pressure increased 8 to 10 mm. at various observations. The pulse pressure remained unchanged.

Patient 5. The increase of systolic pressure varied between 12 and 18 mm. The pulse pressure was unchanged, and the pulse rate was variable.

Patient 6.—The increase in systolic pressure varied between 13 and 20 mm. The pulse pressure before taking the gland was 35; during its administration it was between 45 and 65, and the pulse rate averaged 86.

Patient 7.—The systolic pressure increase averaged 16 mm. The pulse pressure was unchanged. Diarrhea developed after taking the gland extract for two weeks, and it was therefore discontinued.

Patient 8.—This patient suffering with chronic nephritis and low blood pressure was one of the few patients decidedly improved by the action of the gland. The systolic pressure estimated several times before taking the preparation never exceeded 105 mm. of mercury. It rose a short time after the use of the extract to 112; two days later it rose to 120, and henceforth varied between 120 and 125. The diastolic pressure rose synchronously with the systolic. The secretion of urine was decidedly increased, according to the report of the patient, and the subjective symptoms were also markedly alleviated, so that he felt better than at any time during the past several years. The pulse rate also showed an increase, rising from 64 to 92 beats per minute. One week after discontinuation of the drug the pressure was 115 and in two weeks back to 105.

Patient 9.—This patient, with a more elevated pressure than the majority of the individuals studied, showed in nine days an increase in pressure equal to 27 mm. of mercury, the pressure rising to 155 systolic and 90 diastolic. The pulse rate increased to 106. The pituitary extract was immediately stopped.

PATIENT 10.—This patient showed an increase of systolic pressure of 20 mm., but as a severe diarrhea developed the treatment was discontinued.

PATIENT 11.—The systolic pressure was increased, the increase ranging between 12 and 20 mm. of mercury. The pulse pressure ratio remained unchanged. Two weeks after cessation of the drug the systolic pressure had returned to previous figures.

PATIENT 12.—The increase of systolic pressure varied between 15 and 20 mm. of mercury. The diastolic pressure did not show a corresponding increase. The pulse rate was also increased, averaging about 95 beats per minute. Two days after stopping the drug the systolic pressure was down 5 mm. In twelve days it was 5 mm. higher than before starting the experiement. Eighteen days it was approximately at the same level as at the beginning of the drug treatment.

PATIENT 13.—The blood pressure increased from 123 systolic (70 diastolic) to 135 systolic (80 diastolic) in twelve days, when the treatment was stopped on account of diarrhea. The pulse rate increased 15 beats per minute.

Subsequent observations after discontinuation of pituitary extract in these patients showed a tendency for the pressure to return to its previous level after a lapse of about two weeks. This fall occurred gradually so far as could be determined.

Five students took the glandular extract for a week. Four showed a rise in systolic pressure of 4, 10, 15 and 17 mm. of mercury respectively without a corresponding rise in diastolic pressure. One showed no change in the systolic or diastolic pressure. In two of these men no change in the pulse rate occurred, while in the other three there was an increase of 10, 10, and 20 beats per minute. Three noted diuresis; the two that did not note this effect had a rise of 4 and 17 mm. respectively. One man had a slight diarrhea, while 2 had a severe diarrhea, which was worse in the man whose pressure went up the most. Examinations of the urine of the 18 patients were made, and at no time was sugar demonstrated by Fehling's test.

RECAPITULATION. Eighteen individuals were given the dried extract of the whole pituitary gland without other medication. The following effects were noted:

1. Blood pressure: Seventeen showed a rise in systolic blood pressure, the greatest rise being 28 mm. of mercury. Usually a corresponding rise in diastolic pressure occurred, though rarely it remained at the same height as before taking the extract or even became lower.

2. Pulse rate: The changes in the pulse rate were inconstant; an increase was generally observed, though in 2 individuals the rate was decidedly decreased.

3. Diuresis: Six individuals noted a diuretic effect. The extent, absence, or presence of this symptom could not be accurately determined. The urine showed no particular change except in one case (8). Glycosuria was never observed.

4. Intestinal tract: Diarrhea developed in 7 cases, and 4, previously costive, had daily movements during the period of taking the drug.

5. Subjective symptoms: Four individuals were apparently much benefited by the rise in pressure and general stimulative effect of the glandular extract upon the unstriated muscle, and one person was benefited through the diuretic effect of the extract. In the remaining patients there was little effect noted except by those who developed the rather annoying diarrhea.

CONCLUSION. Prolonged administration of extracts of the pituitary gland exert a distinct pressor effect upon the peripheral vascular apparatus, which persists for an appreciable time after discontinuation of the drug. This is apparently the only consistent affect following continued administration of the gland *per oram;* other results are variable and indefinite.

TUBERCULIN THERAPY IN SURGICAL TUBERCULOSIS, WITH THE CORRECT DOSAGE ACCURATELY DETERMINED BY THE CUTANEOUS REACTION.

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In 1910 White and Van Norman[1] reported a method of determining, by means of a cutaneous reaction, the correct therapeutic dosage of tuberculin for subcutaneous injection. The method was adopted in the surgical and gynecological wards of St. Francis Hospital, Pittsburgh, and has been followed in the treatment of twenty-eight cases of surgical tuberculosis. A more recent article[2] by the same writers confirms their previous work.

Starting with the theory that much of the benefit derived from tuberculin therapy is due to the reaction on the part of the body cells produced by tuberculin rather than to an induced tolerance to it, the method is based on the variation in susceptibility of different individuals to the action of tuberculin on the skin and when injected into the tissues. The optimum dose, as determined by this method, is the quantity of tuberculin required to produce the greatest local, general, and focal reaction without producing consitutional symptoms, such as rise of temperature, malaise, and other evidences of overdosage.

The dose for each individual is determined according to that

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[1] Arch. Int. Med., 1910, vi, 449.

[2] Ibid., 1912, ix, 114.